

### Definition

A weight change in adults requires evaluation for potential secondary causes if the loss or gain of total body weight cannot be attributed to purposeful alterations in diet or activity. There are few data, however, to specify the exact weight change that is clinically significant. Weight loss is considerably more indicative of underlying pathology than is weight gain. For example, a minimum loss of 7% of body weight in less than 6 months represents a potentially serious symptom. As the loss or gain approaches 25% of body weight, morbidity and mortality rise more rapidly regardless of the cause.

### Technique

Weight loss or gain in our society has major financial and medical implications, as witnessed by the plethora of popular diets and the relationship of weight change to health and disease. Thus the patient often volunteers information in this area and presents more frequently with complaints of weight gain rather than loss. Initially, by an open-ended question, the patient should be asked to describe the weight change and the circumstances surrounding it. The most important subsequent details are the usual weight, present weight, the time course of the weight change, and any changes in appetite. If the patient is not sure of these crucial components, it is often helpful to ask about a change in dress or belt size, or weights at memorable events such as graduation, marriage, military service, and vacation times. In some instances, relatives and friends may need to be questioned to expand or confirm areas of uncertainty.

Once a weight change is established, the percentage change from the previous body weight as well as "ideal body weight" should be recorded, along with the time span. Subsequent questions should ascertain any predominant body location of the weight change. For example, primary changes in body fluid are often first noticed in the periphery. Information about changes in body fluid or tissue mass can also be obtained from a thorough nutritional assessment. Dietary questions need to be specific, such as the number and kinds of meals recently and routinely consumed; this information should be obtained from the patient and, when possible, from the individual who usually prepares the meals. Also important are snacks, alcohol consumption, and the socioeconomic environment. In the elderly and handicapped, the inability to obtain, properly refrigerate, and cook food may be major contributors to malnutrition.

Additional symptoms relating to weight loss or gain and potential underlying diseases are shown in Tables 210.1 and 210.2. These symptoms, while focused and discriminatory, do not lessen the need for a comprehensive history. For a patient with weight loss, decreased intake and nausea increase the probability of finding an underlying cause. In

contrast, for a patient with weight gain, increased intake is usually not associated with an underlying disease. In either case, appetite changes should be pursued in detail (e.g., "Has the change in appetite been similar for each meal? Has there been a change in the meal preparation? Has the ability to smell or taste food changed?") About 65% of patients with weight loss will be found to harbor disease, compared to less than 1% of those with weight gain.

### Basic Science

A loss or gain in weight may represent different pathophysiologic processes even when they occur in the same

**Table 210.1**  
Selected Symptoms Associated with Weight Loss

#### Decreased intake

Nausea  
Anorexia  
Dysphagia  
Dyspepsia  
Dyspnea  
Cough  
Fever  
Body-image changes  
Menstrual changes  
Drug and alcohol use  
Psychological changes

#### Decreased absorption

Abdominal pain  
Diarrhea

#### Increased metabolic requirements

Symptoms of increased catecholamine effect  
Fever

#### Increased output

Vomiting  
Diarrhea  
Polyuria

**Table 210.2**  
Selected Symptoms Associated with Weight Gain

#### Increased intake

Hyperphagia  
Drug and alcohol use  
Cigarette discontinuance  
Headache  
Visual difficulties  
Psychological changes

#### Decreased output (fluid retention)

Dyspnea  
Drug use  
Edema

disease. For example, diabetic patients may gain weight through increased intake or lose weight through impaired metabolism, absorption, and increased urinary calorie losses. In patients with weight loss, the clinical characteristics can be conveniently categorized into four predominant mechanisms: decreased intake, decreased absorption, increased metabolic requirements, and/or increased loss of nutrients.

#### *Weight Loss: Decreased Intake*

Patients with decreased intake frequently have a greater decrease in protein than calories due to the expense and neglect of protein of high biologic value (animal protein) in the diet. If carbohydrates are consumed, the associated insulin levels lead to diminished lipid and amino acid utilization as well as diminished availability for visceral protein synthesis. For example, a lack of methionine, a lipoprotein precursor, may lead to impaired fat mobilization, fatty infiltration of the liver, and hepatomegaly. As protein availability diminishes, muscle atrophy begins and usually becomes apparent in the temporalis and medial thigh areas. Without essential amino acids, fatigue, pellagra-like dermatitis, and/or dry depigmented skin and brittle hair may develop. As the deficiency advances, albumin, hematocrit, and transferrin levels fall. A decreased albumin results in a lowering of the oncotic pressure, and peripheral edema, ascites, and hypotension may occur. In patients with a reduced intake of protein and other nutrients (carbohydrates and fats), many of the physiologic and clinical correlates of a protein-only deficiency become much less apparent (i.e., hepatomegaly and ascites are rare).

Appropriate energy adaptation to weight loss in protein-calorie malnutrition results, in part, from a reduction in insulin secretion; decreased insulin secretion allows lipolysis and gluconeogenesis to occur. These processes are accentuated by glucagon, cortisol, and growth hormone stimulation. In muscle, protein synthesis is curtailed, and in general, metabolism is reduced by a decrease in the production of triiodothyronine (T3) from thyroxine (T4), along with a decrease in the T3 receptors and catecholamines. This overall improved utilization of fat and protein in protein-calorie malnutrition (as opposed to a protein-only deficiency) results in a relatively higher albumin level (greater than 2.8 gm/dl). Consequently, edema is not found unless the protein-calorie malnutrition is severe. Clinical signs indicate the contraction of lean body mass and adipose tissue such as a diminution of subcutaneous fat in the triceps and deltoid skin fold areas. The skin becomes dry and baggy, and vital signs may become lower than normal with a decrease in skeletal muscle mass.

In protein-only and protein-calorie malnutrition, tissue loss results in a reduction in intracellular nitrogen, potassium, magnesium, and phosphorus, as well as a reduction in extracellular sodium and chloride. There is also an exchange of intracellular muscle potassium and magnesium for plasma sodium, as potassium and magnesium move out of the cell and are excreted by the kidney. In this setting the clinical signs of weakness, tremor, polyuria, and cardiac arrhythmias may be the result of decreased potassium and magnesium. In protein-only deficiency, sodium and extracellular fluid may increase as a result of the accompanying hypoalbuminemia and secondary aldosteronism; also, vitamin A deficiency may be manifest by ocular lesions such as night blindness and xerosis of the conjunctiva and cornea.

Other vitamin deficiencies are variable, but should be carefully sought.

#### *Weight Loss: Decreased Absorption*

Patients with a decreased absorption of nutrients from the small intestine usually have an underlying disease that leads to a predominant reduction in lipids. When a reduction in protein-only or protein-calorie nutrients (carbohydrates, fats) occurs, the clinical manifestations of weight loss are similar to those described above. Malabsorption of any nutrient may result from defects in the luminal, mucosal, or secretory phases of food absorption. For example, predominant fat malabsorption may be due to decreased lipolysis and micellar formation (luminal phase), decreased esterification and chylomicron formation (mucosal phase), and/or decreased lipoprotein secretion and lymphatic transport (secretory phase). The clinical manifestation of these defects usually includes steatorrhea in which the stool may contain unabsorbed dietary fatty acids, bile acids, or both. Patients often complain of an excessively large quantity or sticky stools. Unabsorbed fatty acids in the colon are converted by the intestinal bacteria to hydroxy fatty acids that stimulate excessive electrolyte and fluid secretion. The result is diarrhea, poor skin turgor, and hypotension, often with a concomitant loss of bicarbonate with metabolic acidosis and compensatory hyperpnea. Other clinical manifestations may result from a loss of the lipid-soluble vitamins (A, D, E, and K) as well as B<sub>12</sub> and folate. These patients may have dermatitis, osteopenia, bleeding, anemia, and peripheral neuropathy. Other major nutrient losses, such as carbohydrates, may occur with a conversion in the colon to osmotically active fatty acids and resultant diarrhea. Protein losses in this setting produce the same clinical characteristics as seen in protein-only malnutrition.

#### *Weight Loss: Increased Metabolic Requirements*

Patients with increased metabolic requirements may need a large calorie expenditure due to the demands of increased motor activity, increased metabolic rate, or both. The molecular mechanisms responsible for the associated weight loss are not well understood, but are probably due to a variety of hormone effects on multiple metabolic pathways. For example, thyroid hormone increases tissue sodium-potassium adenosine triphosphatase (ATPase) activity resulting in an excess synthesis of ATPase and concomitant loss of heat energy. Thyroid hormone also increases beta-adrenergic receptor sensitivity to catecholamines. Since metabolic regulation is also under neural control, an activation of the sympathetic nervous system results in increased circulating levels of catecholamines and glucagon and impaired insulin secretion. The clinical signs of catecholamine excess, while self-protective acutely, may chronically become self-destructive with diaphoresis, tachycardia, and hypertension. Some patients also develop diarrhea and lose nutrients in the stool.

#### *Weight Loss: Increased Loss of Nutrients*

Patients with an increased loss of nutrients may present a clinical picture characteristic of the particular nutrient deficiency. For example, loss of blood or urinary loss of pro-

teins may result in those signs described for decreased intake and protein-only losses. Losses of electrolytes and calories from diarrhea may result in the signs described under malabsorption. In many diseases, multiple mechanisms are operative; therefore, the symptoms, signs, and laboratory parameters must be synthesized carefully.

#### *Weight Gain: Increased Intake*

The patient with weight gain is unlikely to have an underlying organic disease. If a disease is present, the clinical characteristics usually result from two mechanisms: increased intake and/or decreased output (i.e., fluid retention). Patients with increased intake usually manifest physical signs similar to primary (exogenous) obesity. Metabolic changes may include hyperinsulinemia, reduction in fat and muscle cell sensitivity to insulin (decreased receptors), decreased glucose tolerance, and an increase in glucocorticoid production and metabolism. Overall physical signs tend to relate to the premorbid condition. For example, patients who have been previously underweight or normal weight or have adult-onset obesity generally add mass in the central regions such as the trunk, whereas patients who have had lifelong obesity tend to have peripheral as well as central adiposity. Exceptions to this finding occur in the central obesity of Cushing's syndrome or when superimposed fluid retention occurs in the extremities.

#### *Weight Gain: Decreased Output (Fluid Retention)*

Patients with decreased output in proportion to intake, especially fluid, can have superimposed gains or losses of lean body tissue mass. With normal plasma oncotic pressure, a decrease in fluid excretion such as in renal insufficiency often results in a positive balance of extracellular fluid, sodium and chloride, and weight gain. Such an increase may lead to cardiovascular overload and edema, hepatomegaly, and jugular venous distention when the right heart and venous capacitance are exceeded. Fluid increases can also result in cardiomegaly, hypertension, and pulmonary effusions when the capacity of the left heart and arterial impedance are exceeded. In this setting, atrial and ventricular gallops may be heard on either side of the heart. Mixed right and left heart physical signs are common.

### **Clinical Significance**

The differential diagnosis of weight loss and gain are shown in Tables 210.3 and 210.4. Although diseases cannot always be compartmentalized by their pathophysiologic mechanisms and occasionally overlap, it is often necessary to initially formulate a broad-based differential diagnosis.

#### *Weight Loss: Decreased Intake*

A decreased intake may occur due to an inability to obtain or ingest food. The inability to obtain adequate protein or protein-caloric nutrition is a significant problem, especially in Third World countries. Kwashiorkor and marasmus, respectively, are the end result. Hospitalized patients also have a high prevalence of a "kwashiorkor-like" syndrome. It is estimated that 25 to 50% of patients given prolonged in-

**Table 210.3**  
Differential Diagnosis of Weight Loss

#### **Decreased intake**

Malignancy (esp. pulmonary, lymphoma, GI, renal)  
Chronic debilitating diseases (esp. severe COPD, CHF, rheumatoid arthritis)  
Mouth and throat disorders (e.g., poor dentition, stomatitis)  
Esophageal obstruction (e.g., achalasia)  
Gastric ulcer made worse with food  
Duodenal ulcer with outlet obstruction  
Liver disease (e.g., advanced cirrhosis)  
Renal failure  
Infections (e.g., tuberculosis)  
Endocrine disorders (e.g., Addison's disease, hypopituitarism)  
Drugs (e.g., digitalis, antineoplastic agents) and alcohol  
Psychoneurologic (e.g., anorexia nervosa, bulimia, depression, stroke, CNS neoplasm)

#### **Decreased absorption**

Postgastrectomy syndrome  
Intestinal disease (e.g., Crohn's disease, ulcerative colitis)  
Cholestatic disease  
Pancreatic exocrine disease  
Infections (e.g., giardiasis)  
Diabetic enteropathy  
Drugs

#### **Increased metabolic requirements**

Hyperthyroidism  
Pheochromocytoma  
Major surgery  
Fever  
Mania

#### **Increased output**

Diabetes mellitus  
Chronic vomiting, diarrhea, bleeding  
Fistulous or catheter drainage  
Nephrotic syndrome

**Table 210.4**  
Differential Diagnosis of Weight Gain

#### **Increased intake**

Central nervous system disorders  
Withdrawal from cigarettes  
Drugs (cyproheptadine, oral contraceptives, phenothiazines)  
Mechanical (e.g., trauma, pseudotumor cerebri)  
Neoplastic (e.g., craniopharyngioma, glioma)  
Inflammatory (e.g., tuberculosis, sarcoidosis)  
Endocrine disorders  
Polycystic ovary disease  
Hyperinsulinism (Insulinoma)  
Hyperadrenocorticism (e.g., exogenous use of steroids, Cushing's)  
Hypothyroidism  
Psychologic disturbance (e.g., depression)

#### **Decreased output**

Fluid retention  
Inappropriate antidiuretic hormone (e.g., brain and lung diseases, drugs such as chlorpropamide)  
Drugs (e.g., oral contraceptives, some antihypertensive agents)  
Congestive heart failure  
Nephrosis and nephrotic syndrome  
Cirrhosis  
Myxedema  
Beriberi  
Fat accumulation  
Multiple lipomatosis  
Partial lipodystrophy



fusions of intravenous saline and dextrose without regard for amino acid supplementation develop this protein-only deficiency syndrome. In this setting it is not unusual for albumin levels to drop within 3 to 5 days of hospital admission, depending on the degree of catabolism associated with surgery, fever, and any secondary diseases.

Malignancy is the most common disease producing weight loss. The weight loss is usually a result of anorexia. Although pancreatic carcinoma is classically associated with major weight loss (20 to 30% of ideal body weight), this tumor is not common and may first present with silent jaundice or abdominal pain. Pulmonary and gastrointestinal malignancies are the most common tumors associated with weight loss and anorexia. Chronic debilitating disease may affect intake because of a decreased appetite, an inability to prepare food, or both. Obstruction and/or pain associated with eating may also limit intake in patients who have a peptic ulcer or a neoplastic growth that invades or compresses the stomach or intestine. Although granulomatous infections such as tuberculosis can cause weight loss, there is usually other evidence of systemic disease, such as fever. Endocrine disorders such as panhypopituitarism and Addison's disease are associated with anorexia presumably due to cortisol deficiency. Finally, neuroendocrine abnormalities may result from drugs, central nervous system disease, or both. Although these abnormalities are relatively rare, marked weight loss in adolescents and young adults due to anorexia nervosa-bulimia syndromes appears to be increasing. Their presenting complaints often include irregular or absent menstruation, constipation, and cold intolerance. Their physical and laboratory abnormalities can often be attributed to protein-calorie and electrolyte malnutrition, of which hypokalemia may be life threatening.

#### *Weight Loss: Decreased Absorption*

Multiple abnormalities are seen in the malabsorption syndromes. Decreased absorption may occur with a single or multiple nutrient deficiency, depending on the site of intestinal malfunction. Consequently, symptoms and signs tend to be variable. In fat malabsorption, the traditional symptom of a soft, greasy, malodorous stool that floats may or may not be present. Many patients complain of vague abdominal pain, borborygmi and/or abdominal distention with normal stools or one large, bulky stool per day. Floating stools are the result of increased air in the stool rather than fat. Although specific diseases of the stomach, small intestine, gallbladder, and pancreas have typical clinical characteristics, early disease can be unimpressive except for nonspecific intermittent abdominal distention. For example, *Giardia lamblia* may parasitize the small intestine and remain asymptomatic or produce severe symptoms. In contrast, other diseases will rarely have the clinical manifestations of malabsorption without other signs and symptoms. For example, diabetic patients with autonomic neuropathy usually also have orthostatic hypotension, impotence, and hypohidrosis.

#### *Weight Loss: Increased Metabolic Demand*

Multiple mechanisms may be operative in endocrine disorders such as hyperthyroidism. In these patients, there is an increased metabolic rate; fat malabsorption is rare. Infrequently, patients have gained weight in hyperthyroidism; for example, at least 15% of adolescents gain weight with

hyperthyroidism and only 50% lose weight. In the elderly patient, typical symptoms and signs of increased thyroid activity may be blunted or absent (apathetic hyperthyroidism). Their predominant complaints are often weight loss and fatigue, suggesting malignancy. Patients with pheochromocytoma may also present with weight loss related to an increased metabolic demand. Other causes of increased metabolic demand, such as surgery, fever, or mania, are usually evident on complete history and physical examination.

#### *Weight Loss: Increased Output*

When diarrhea occurs with hyperthyroidism, weight loss may be exacerbated. In a patient with a surgically abbreviated small intestine, the development or exacerbation of diarrhea may worsen the severity of nutrient loss; if the albumin is reduced, there may be a net loss of oncotic force and a gain rather than loss of weight. In diseases such as diabetes mellitus, fluid and calorie losses occur through the osmotic diuretic effect of hyperglycemia and the catabolic effect of hypoinsulinemia; a net gain of fluid and calories may occur, however, if exogenous insulin administration is required or if renal insufficiency supervenes.

#### *Weight Gain: Increased Intake*

Weight gain may be caused by increased intake or decreased output (i.e., fluid retention). Increased intake is often due to increased appetite. Central nervous system (CNS) disorders, however, may rarely cause a major gain in weight via effects on the hypothalamus and neurotransmitter systems. In the absence of symptoms such as headache and visual field disturbances, an extensive CNS evaluation for weight gain is not warranted. Patients with endocrine disorders such as hypothyroidism and Cushing's syndrome generally demonstrate other clinical features in addition to weight gain.

#### *Weight Gain: Decreased Output (Fluid Retention)*

Fluid retention is a frequent cause of weight gain. Medicines such as nonsteroidal inflammatory drugs are a commonly missed cause of fluid retention. Excess antidiuretic hormone, not generally apparent until hyponatremia is detected, is a less frequent cause. Advanced congestive heart failure, cirrhosis, and myxedema are usually clinically apparent causes, but nephrosis may be clinically occult before the urinalysis. Rare disorders of nutrient accumulation (e.g., lipodystrophies) may be attributed to accumulations of fat that may or may not be apparent by history.

Although the clinical characteristics of the above causes of weight loss or gain are protean and the number of potential laboratory investigations are considerable, a complete history, physical examination, and directed laboratory evaluation are most efficacious and cost effective. The screening hemogram, urinalysis, and chemistry profile (electrolytes, glucose, renal, and liver function tests and albumin) are sufficient evaluation for the etiology and complications of most patients with isolated weight gain. For patients with weight loss, a chest roentgenogram should be added if there are respiratory symptoms or an increased risk of pulmonary malignancy. In the elderly patient with

weight loss, apathetic hyperthyroidism, a potentially correctable cause, should be excluded by obtaining levels of free thyroxine and total triiodothyronine (T3).

## References

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